FIGURE 1

FIGURE 2

1	M	S	V	G	A	M	K	K	G	V	G	R	A	V	G	L	G	G	G	S	20
21	G	C	Q	A	T	E	E	D	P	L	P	D	C	G	A	C	A	P	G	Q	40
41	G	G	R	R	W	R	L	P	Q	P	A	W	V	E	G	S	S	A	R	L	60
61	W	E	Q	A	T	G	T	G	W	M	D	L	E	A	S	L	L	P	T	G	80
81	P	N	A	S	N	T	S	D	G	P	D	N	L	T	S	A	G	S	P	P	100
101	R	T	G	S	I	S	Y	I	N	I	I	M	P	S	V	F	G	T	I	C	120
121	L	L	G	I	I	G	N	S	T	V	I	F	A	V	V	K	K	S	K	L	140
141	H	W	C	N	N	V	P	D	I	F	I	I	N	L	S	V	V	D	L	L	160
161	F	L	L	G	M	P	F	M	I	H	Q	L	M	G	N	G	V	W	H	F	180
181	G	E	T	M	C	T	L	I	T	A	M	D	A	N	S	Q	F	T	S	T	200
201	Y	I	L	T	A	M	A	I	D	R	Y	L	A	T	V	H	P	I	S	S	220
221	T	K	F	R	K	P	S	V	A	T	L	V	I	C	L	L	W	A	L	S	240
241	F	I	S	I	T	P	V	W	L	Y	A	R	L	I	P	F	P	G	G	A	260
261	V	G	C	G	I	R	L	P	N	P	D	T	D	L	Y	W	F	T	L	Y	280
281	Q	F	F	L	A	F	A	L	P	F	V	V	I	T	A	A	Y	V	R	I	300
301	L	Q	R	M	T	S	S	V	A	P	A	S	Q	R	S	I	R	L	R	T	320
321	K	R	V	T	R	T	A	I	A	I	C	L	V	F	F	V	C	W	A	P	340
341	Y	Y	V	L	Q	L	T	Q	L	S	I	S	R	P	T	L	T	F	V	Y	360
361	L	Y	N	A	A	I	S	L	G	Y	A	N	S	C	L	N	P	F	V	Y	380
381	I	V	L	C	E	T	F	R	K	R	L	V	L	S	V	K	P	A	A	Q	400
401	G	Q	L	R	A	V	S	N	A	Q	T	A	D	E	E	R	T	E	S	K	420
421	G	T																			422

FIGURE 3

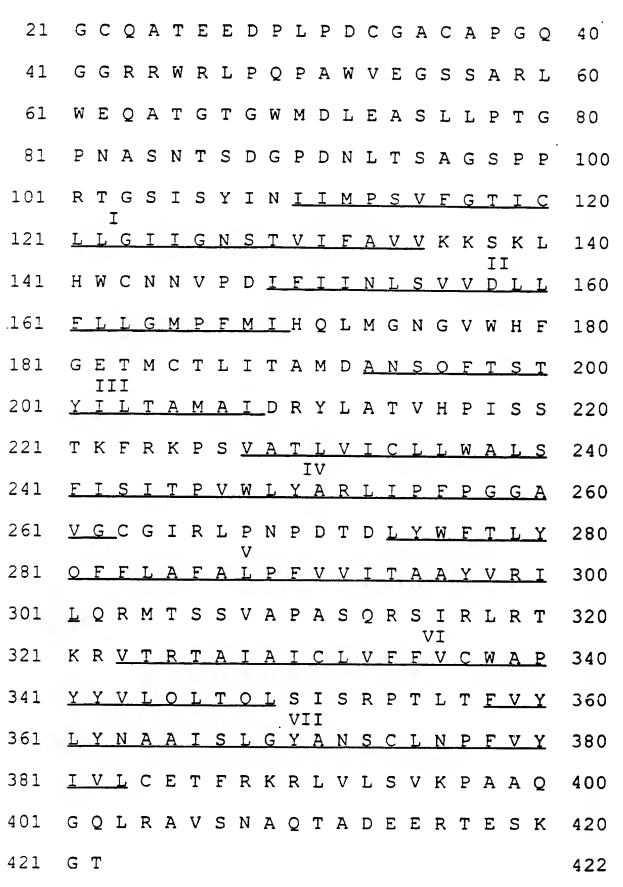


FIGURE 4

1 GCAGGCGACCTGCACCGGCTGCATGGATCTGCAAACCTCGTTGCTGTCCACTGGCCCCAA 60
61 TGCCAGCAACATCTCCGATGGCCAGGATAATCTCACATTGCCGGGGTCACCTCCTCGCAC 120
121 AGGGAGTGTCTCCTACATCAACATCATTATGCCTTCCGTGTTTGGTACCATCTGTCTCCT 180
181 GGGCATCGTGGGAAACTCCACGGTCATCTTTGCTGTGGTGAAGAAGTCCAAGCTACACTG 240
241 GTGCAGCAACGTCCCCGACATCTTCATCATCAACCTCTCTGTGGTGGATCTGCTCTTCCT 300
301 GCTGGGCATGCCTTTCATGATCCACCAGCTCATGGGGAACGGCGTCTGGCACTTTGGGGA 360
361 AACCATGTGCACCCTCATCACAGCCATGGACGCCAACAGTCAGTTCACTAGCACCTACAT 420
421 CCTGACTGCCATGACCATTGACCGCTACTTGGCCACCGTCCACCCCATCTCCTCCACCAA 480
481 GTTCCGGAAGCCCTCCATGGCCACCCTGGTGATCTGCCTCCTGTGGGCGCTCTCCTTCAT 540
541 CAGTATCACCCCTGTGTGGCTCTACGCCAGGCTCATTCCCTTCCCAGGGGGTGCTGTGGG 600
601 CTGTGGCATCCGCCTGCCAAACCCGGACACTGACCTCTACTGGTTCACTCTGTACCAGTT 660
661 TTTCCTGGCCTTTGCCCTTCCGTTTGTGGTCATTACCGCCGCATACGTGAAAATACTACA 720
721 GCGCATGACGTCTTCGGTGGCCCCAGCCTCCCAACGCAGCATCCGGCTTCGGACAAAGAG 780
781 GGTGACCCGCACGGCCATTGCCATCTGTCTGGTCTTCTTTGTGTGCTGGGCACCCTACTA 840
841 TGTGCTGCAGCTGACCCAGCTGTCCATCAGCCGCCCGACCCTCACGTTTGTCTACTTGTA 900
901 CAACGCGGCCATCAGCTTGGGCTATGCTAACAGCTGCCTGAACCCCTTTGTGTACATAGT 960
961 GCTCTGTGAGACCTTTCGAAAACGCTTGGTGTTGTCAGTGAAGCCTGCAGCCCAGGGGCA 1020
1021 GCTCCGCACGGTCAGCAACGCTCAGACAGCTGATGAGGAGAGGACAGAAAGCAAAGGCAC 1080
1081 CTGACAATTCCCCAGTCGCCTCCAAGTCAGGCCACCCCATCAAACCGTGGGGAGAGATAC 1140
1141 TGAGATTAAACCCAAGGCTACCCTGGGAGAATGCAGAGGCTGGAGGCTGGGGGCTTGTAG 1200
1201 CAACCACATTCCAC 1214

FIGURE 5

```
  1  M D L Q T S L L S T G P N A S N I S D G   20
 21  Q D N L T L P G S P P R T G S V S Y I N   40
 41  I I M P S V F G T I C L L G I V G N S T   60
 61  V I F A V V K K S K L H W C S N V P D I   80
 81  F I I N L S V V D L L F L L G M P F M I  100
101  H Q L M G N G V W H F G E T M C T L I T  120
121  A M D A N S Q F T S T Y I L T A M T I D  140
141  R Y L A T V H P I S S T K F R K P S M A  160
161  T L V I C L L W A L S F I S I T P V W L  180
181  Y A R L I P F P G G A V G C G I R L P N  200
201  P D T D L Y W F T L Y Q F F L A F A L P  220
221  F V V I T A A Y V K I L Q R M T S S V A  240
241  P A S Q R S I R L R T K R V T R T A I A  260
261  I C L V F F V C W A P Y Y V L Q L T Q L  280
281  S I S R P T L T F V Y L Y N A A I S L G  300
301  Y A N S C L N P F V Y I V L C E T F R K  320
321  R L V L S V K P A A Q G Q L R T V S N A  340
341  Q T A D E E R T E S K G T *             354
```

FIGURE 6

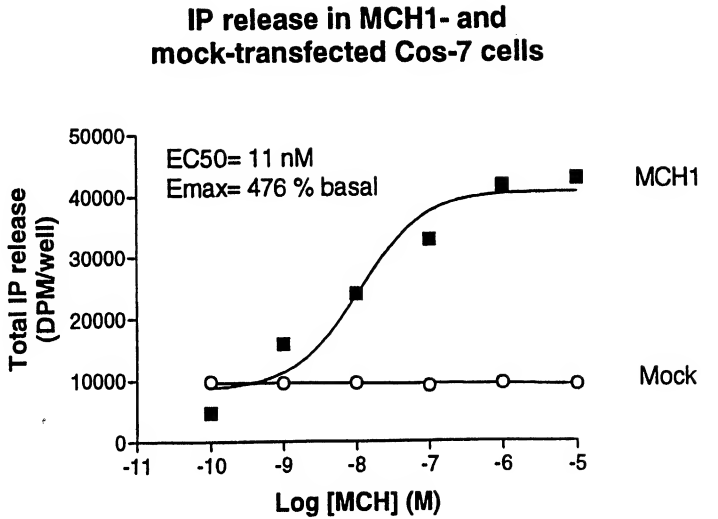
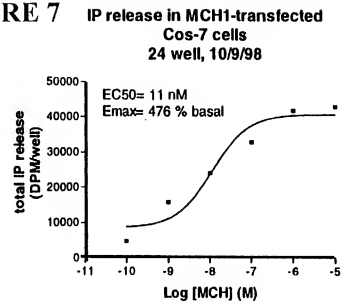
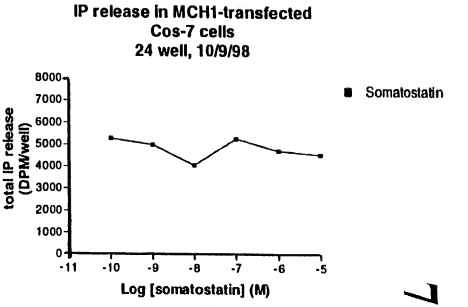
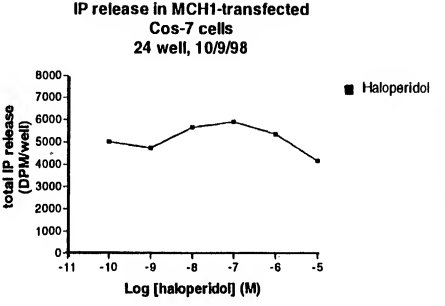


FIGURE 7







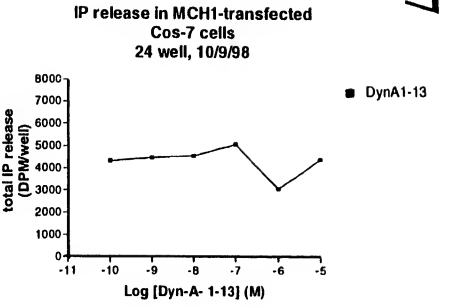
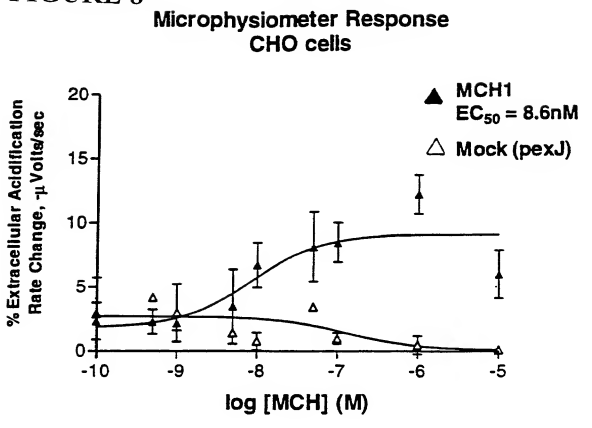


FIGURE 8



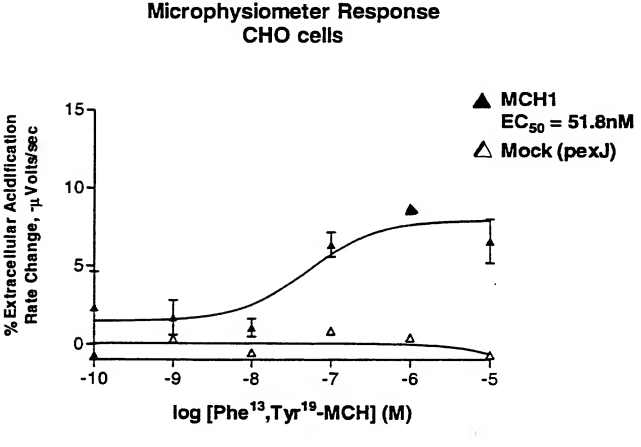


FIGURE 9

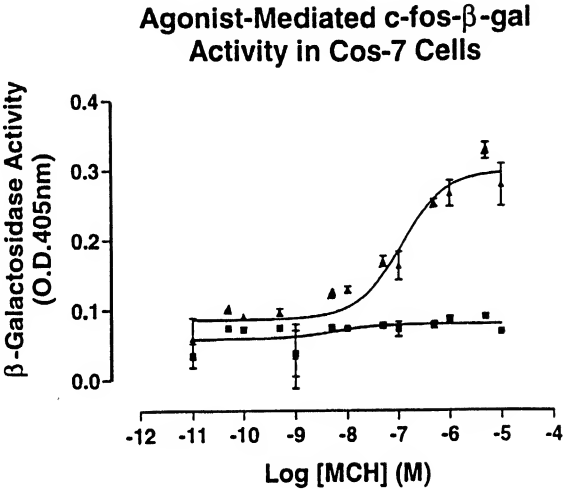
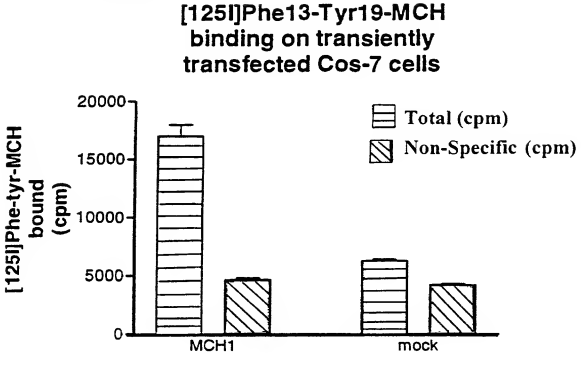


FIGURE 10


[125I]Phe13-Tyr19-MCH
binding on transiently
transfected Cos-7 cells
[125I]Phe-tyr-MCH
bound
(cpm)
20000
15000
10000
5000
0
Total (cpm)
Non-Specific (cpm)
MCH1
mock

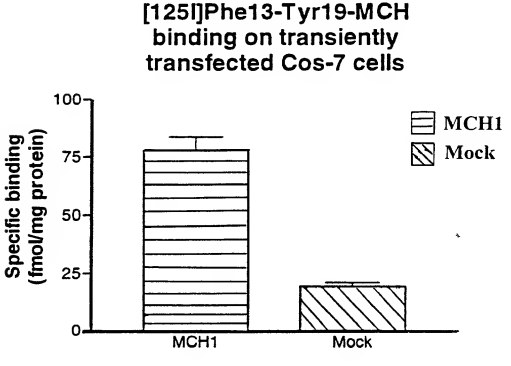

[125I]Phe13-Tyr19-MCH
binding on transiently
transfected Cos-7 cells
Specific binding
(fmol/mg protein)
100
75
50
25
0
MCH1
Mock
MCH1
Mock

FIGURE 11

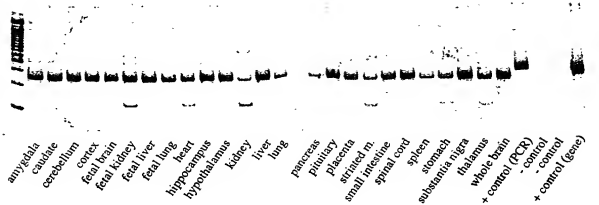


FIGURE 12

```
                1                                                   40
TL231           MSVGAMKKGV  GRAVGLGGGS  GCQATEEDPL  PDCGACAPGQ
R106            MSVGAMKKGV  GRAVGLGGGS  GCQATEEDPL  PDCGACAPGQ
R114            MSVGAaKKGV  GRAVGLGGGS  GCQATEEDPL  PDCGACAPGQ
BO120           ~~~~~~~~~~  ~~~~~~~~~~  ~~~~~~~~~~  ~~~~~~~~~~

               41                                                   80
TL231           GGRRWRLPQP  AWVEGSSARL  WEQATGTGWM  DLEASLLPTG
R106            GGRRWRLPQP  AWVEGSSARL  WEQATGTGWa  DLEASLLPTG
R114            GGRRWRLPQP  AWVEGSSARL  WEQATGTGWa  DLEASLLPTG
BO120           ~~~~~~~~~~  ~~~~~~~~~~  ~~~~~~~~~M  DLEASLLPTG

               81                  100
TL231           PNASNTSDGP  DNLTSAGSPP...
R106            PNASNTSDGP  DNLTSAGSPP...
R114            PNASNTSDGP  DNLTSAGSPP...
BO120           PNASNTSDGP  DNLTSAGSPP...
```

FIGURE 13

1	M	S	V	G	A	M	K	K	G	V	G	R	A	V	G	L	G	G	G	S	20
21	G	C	Q	A	T	E	E	D	P	L	P	D	C	G	A	C	A	P	G	Q	40
41	G	G	R	R	W	R	L	P	Q	P	A	W	V	E	G	S	S	A	R	L	60
61	W	E	Q	A	T	G	T	G	W	A	D	L	E	A	S	L	L	P	T	G	80
81	P	N	A	S	N	T	S	D	G	P	D	N	L	T	S	A	G	S	P	P	100
101	R	T	G	S	I	S	Y	I	N	I	I	M	P	S	V	F	G	T	I	C	120
121	L	L	G	I	I	G	N	S	T	V	I	F	A	V	V	K	K	S	K	L	140
141	H	W	C	N	N	V	P	D	I	F	I	I	N	L	S	V	V	D	L	L	160
161	F	L	L	G	M	P	F	M	I	H	Q	L	M	G	N	G	V	W	H	F	180
181	G	E	T	M	C	T	L	I	T	A	M	D	A	N	S	Q	F	T	S	T	200
201	Y	I	L	T	A	M	A	I	D	R	Y	L	A	T	V	H	P	I	S	S	220
221	T	K	F	R	K	P	S	V	A	T	L	V	I	C	L	L	W	A	L	S	240
241	F	I	S	I	T	P	V	W	L	Y	A	R	L	I	P	F	P	G	G	A	260
261	V	G	C	G	I	R	L	P	N	P	D	T	D	L	Y	W	F	T	L	Y	280
281	Q	F	F	L	A	F	A	L	P	F	V	V	I	T	A	A	Y	V	R	I	300
301	L	Q	R	M	T	S	S	V	A	P	A	S	Q	R	S	I	R	L	R	T	320
321	K	R	V	T	R	T	A	I	A	I	C	L	V	F	F	V	C	W	A	P	340
341	Y	Y	V	L	Q	L	T	Q	L	S	I	S	R	P	T	L	T	F	V	Y	360
361	L	Y	N	A	A	I	S	L	G	Y	A	N	S	C	L	N	P	F	V	Y	380
381	I	V	L	C	E	T	F	R	K	R	L	V	L	S	V	K	P	A	A	Q	400
401	G	Q	L	R	A	V	S	N	A	Q	T	A	D	E	E	R	T	E	S	K	420
421	G	*																			422

FIGURE 14

1	M	S	V	G	A	A	K	K	G	V	G	R	A	V	G	L	G	G	G	S	20
21	G	C	Q	A	T	E	E	D	P	L	P	D	C	G	A	C	A	P	G	Q	40
41	G	G	R	R	W	R	L	P	Q	P	A	W	V	E	G	S	S	A	R	L	60
61	W	E	Q	A	T	G	T	G	W	A	D	L	E	A	S	L	L	P	T	G	80
81	P	N	A	S	N	T	S	D	G	P	D	N	L	T	S	A	G	S	P	P	100
101	R	T	G	S	I	S	Y	I	N	I	I	M	P	S	V	F	G	T	I	C	120
121	L	L	G	I	I	G	N	S	T	V	I	F	A	V	V	K	K	S	K	L	140
141	H	W	C	N	N	V	P	D	I	F	I	I	N	L	S	V	V	D	L	L	160
161	F	L	E	G	M	P	F	M	I	H	Q	L	M	G	N	G	V	W	H	F	180
181	G	E	T	M	C	T	L	I	T	A	M	D	A	N	S	Q	F	T	S	T	200
201	Y	I	L	T	A	M	A	I	D	R	Y	L	A	T	V	H	P	I	S	S	220
221	T	K	F	R	K	P	S	V	A	T	L	V	I	C	L	L	W	A	L	S	240
241	F	I	S	I	T	P	V	W	L	Y	A	R	L	I	F	F	P	G	C	A	260
261	V	G	C	G	I	R	L	P	N	P	D	T	D	L	Y	W	F	T	L	Y	280
281	Q	F	F	L	A	F	A	L	P	F	V	V	I	T	A	A	Y	V	R	I	300
301	L	Q	R	M	T	S	S	V	A	P	A	S	Q	R	S	I	R	L	R	T	320
321	K	R	V	T	R	T	A	I	A	I	C	L	V	F	F	V	C	W	A	P	340
341	Y	Y	V	L	Q	L	T	Q	L	S	I	S	R	P	T	L	T	F	V	Y	360
361	L	Y	N	A	A	I	S	L	G	Y	A	N	S	C	L	N	P	F	V	Y	380
381	I	V	L	C	E	T	F	R	K	R	L	V	L	S	V	K	P	A	A	Q	400
401	G	Q	L	R	A	V	S	N	A	Q	T	A	D	E	E	R	T	E	S	K	420
421	G	T																			422

FIGURE 15

FIGURE 16

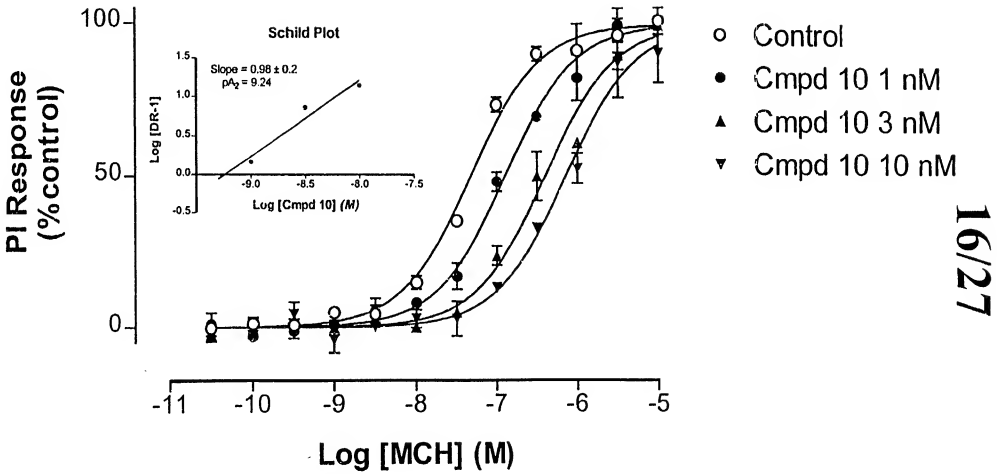

PI Response (%control)
100
50
0
Schild Plot
Slope = 0.98 ± 0.2
pA2 = 9.24
Log [DR-1]
1.5
1.0
0.5
0.0
-0.5
-9.0
-8.5
-8.0
-7.5
Log [Cmpd 10] (M)
-11
-10
-9
-8
-7
-6
-5
Log [MCH] (M)
Control
Cmpd 10 1 nM
Cmpd 10 3 nM
Cmpd 10 10 nM

FIGURE 17

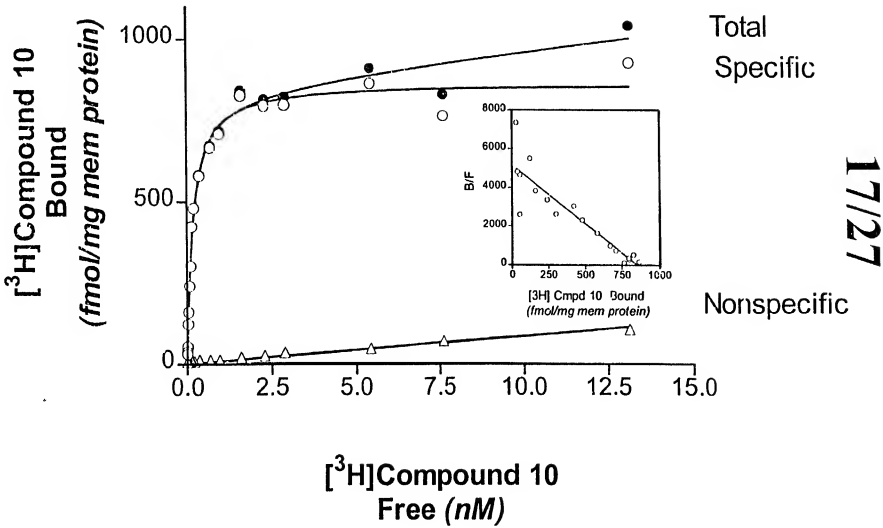

[3H]Compound 10 Bound (fmol/mg mem protein)
1000
500
0
0.0
2.5
5.0
7.5
10.0
12.5
15.0
[3H]Compound 10 Free (nM)
Total
Specific
Nonspecific
B/F
8000
6000
4000
2000
0
250
500
750
1000
[3H] Cmpd 10 Bound (fmol/mg mem protein)

FIGURE 18

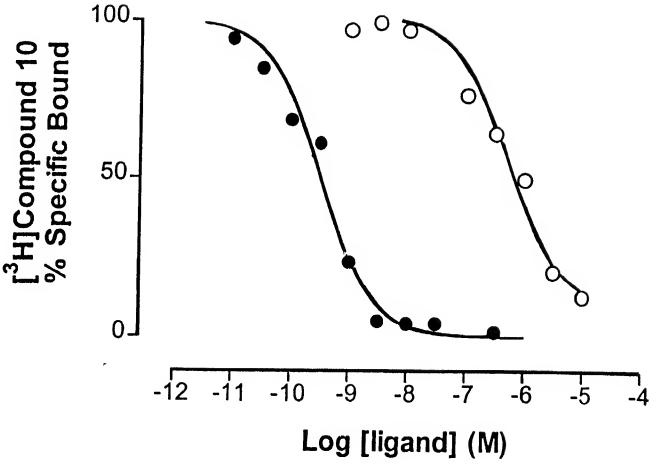
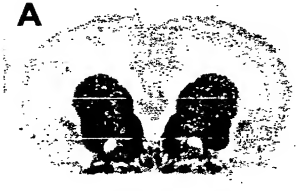


FIGURE 19

Total MCH1 Receptor Binding

Nonspecific binding

A



B

FIGURE 20A

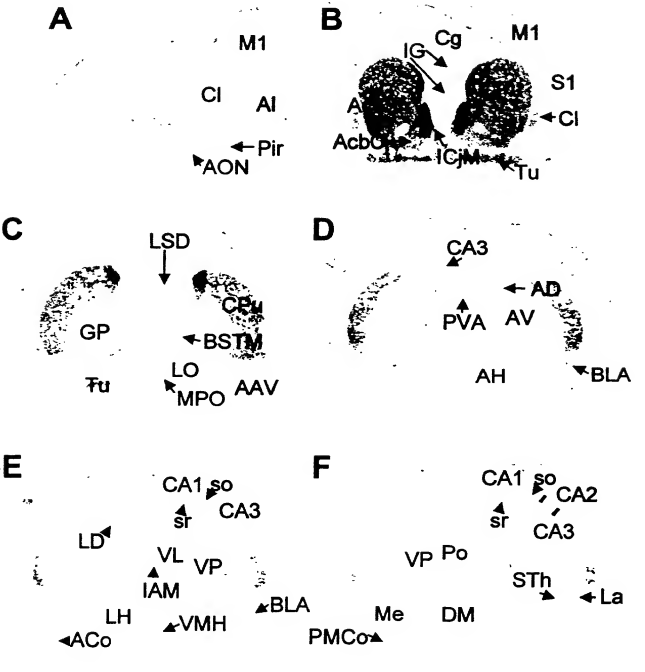

A
M1
Cl
Al
Pir
AON
B
Cg
M1
IG
S1
A
Cl
AcbC
ICjM
Tu
C
LSD
CPu
GP
BSTM
LO
Tu
MPO
AAV
D
CA3
AD
PVA
AV
AH
BLA
E
CA1
so
CA3
sr
LD
VL
VP
IAM
LH
VMH
BLA
ACo
F
CA1
so
CA2
sr
CA3
VP
Po
STh
La
Me
DM
PMCo

FIGURE 20B

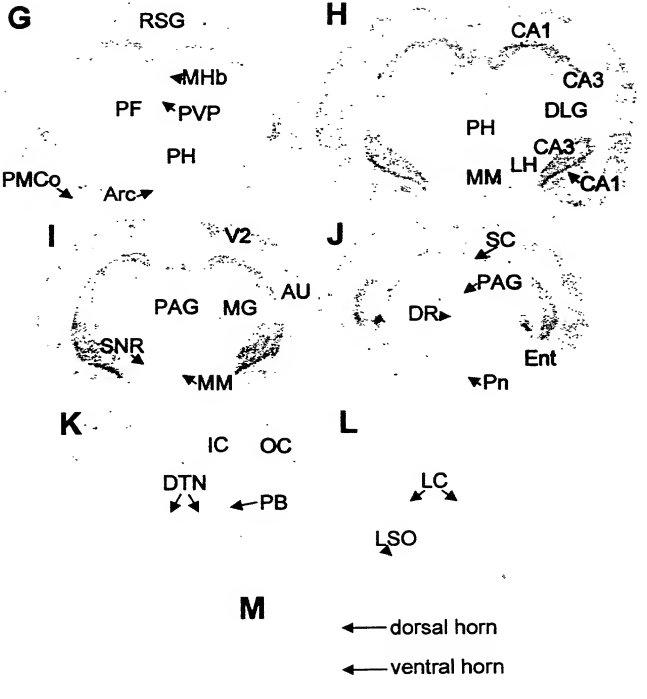
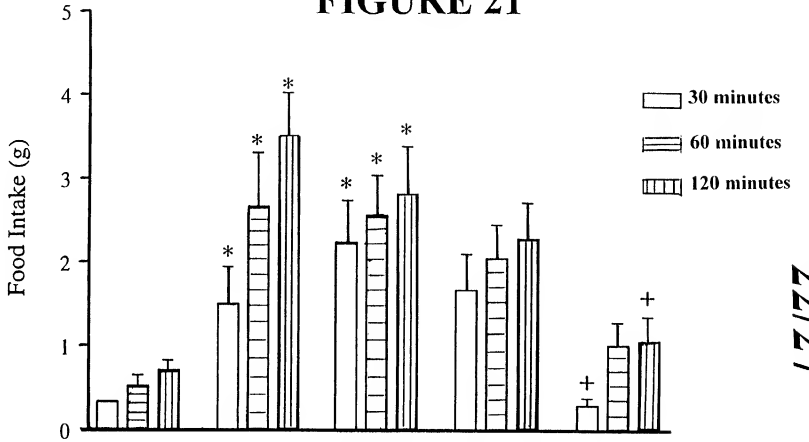

G
RSG
MHb
PF
PVP
PH
PMCo
Arc
H
CA1
CA3
DLG
PH
CA3
LH
MM
CA1
I
V2
AU
PAG
MG
SNR
MM
J
SC
PAG
DR
Ent
Pn
K
IC
OC
DTN
PB
L
LC
LSO
M
dorsal horn
ventral horn

FIGURE 21



* sig. > than vehicle

\+ sig. < than veh+MCH

FIGURE 22

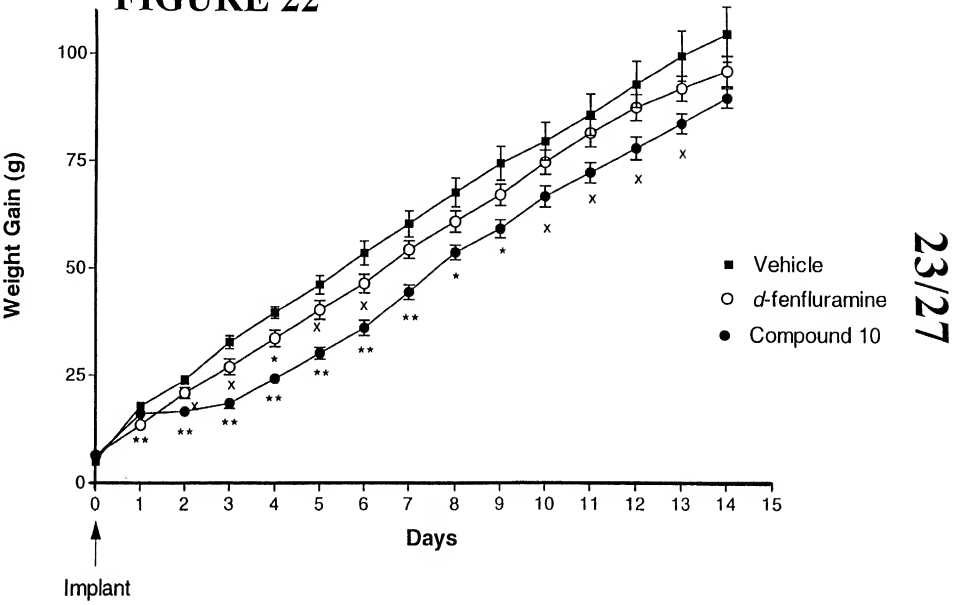


FIGURE 23

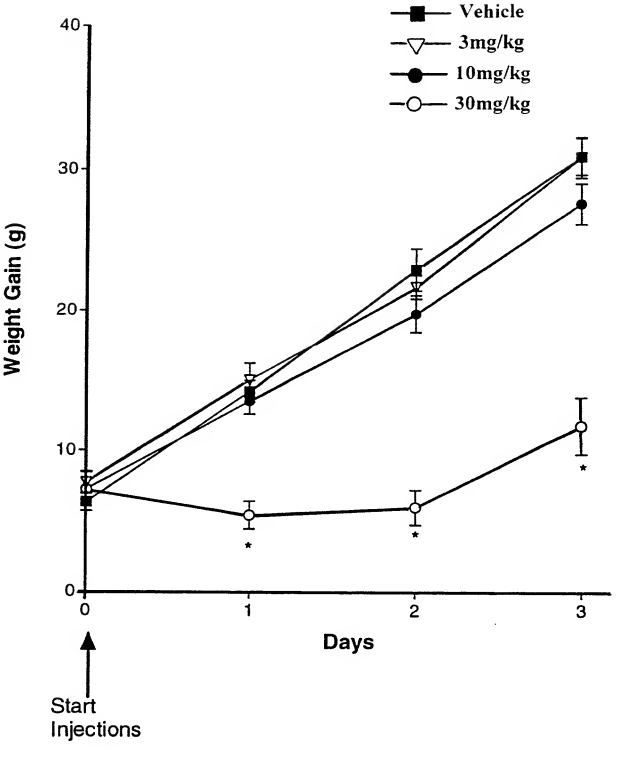


FIGURE 24

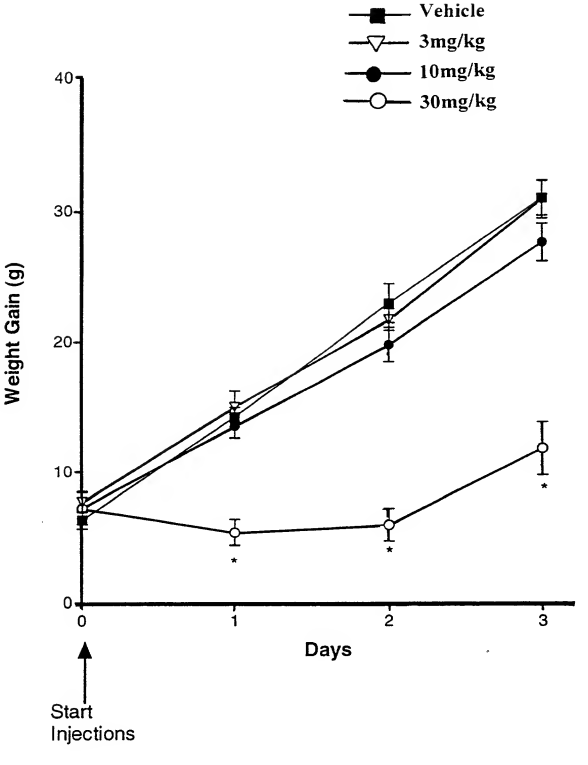


FIGURE 25

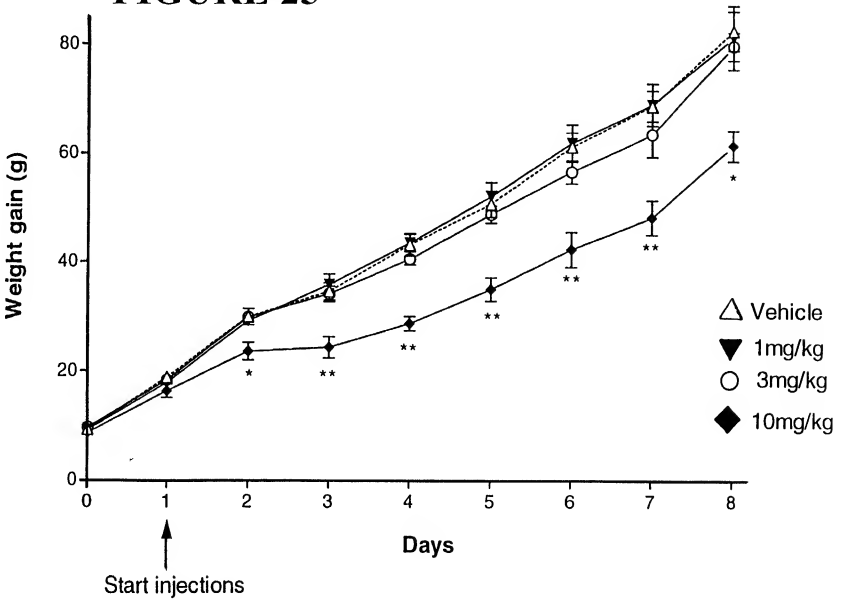
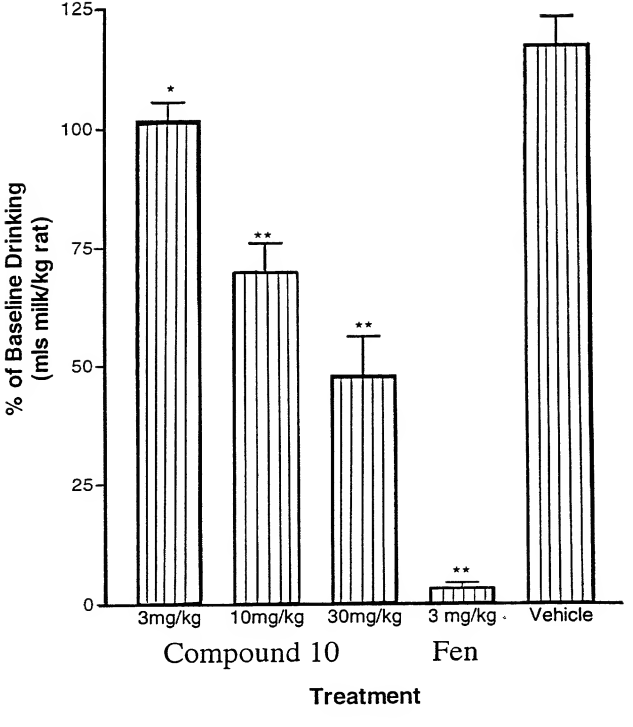


FIGURE 26


125
100
75
50
25
0
% of Baseline Drinking
(mls milk/kg rat)
*
**
**
**
3mg/kg
10mg/kg
30mg/kg
3 mg/kg
Vehicle
Compound 10
Fen
Treatment